Regulation of Mammalian Keratinous Tissue Using N-acyl Amino Acid Compositi ns

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Technical Field

The present invention relates to skin care compositions containing N-acyl amino acid, particularly N-acyl derivatives of Phenylalanine or Tyrosine, their isomers, or their salts in combination with at least one other skin care active selected from sugar amines, vitamin B_3, retinoids, peptides, dialkanoyl hydroxyproline, hexamidine, salicylic acid, and phytosterol. Such compositions are useful for regulating the condition of mammalian keratinous tissue needing such treatments.

Background of the Invention

Currently, there are a number of personal care products that are available to consumers, which are directed toward improving the health and physical appearance of keratinous tissues such as the skin, hair, and nails. The majority of these products are directed to delaying, minimizing or even eliminating skin wrinkling and other histological changes typically associated with the aging of skin or environmental damage to human skin. However, there exists a need for cosmetic agents to prevent, retard, and/or treat uneven skin tone by acting as a lightening or pigmentation reduction cosmetic agent.

Mammalian keratinous tissue, particularly human skin, is subjected to a variety of insults by both extrinsic and intrinsic factors. Such extrinsic factors include ultraviolet radiation, environmental pollution, wind, heat, infrared radiation, low humidity, harsh surfactants, abrasives, etc. Intrinsic factors, on the other hand, include chronological aging and other biochemical changes from within the skin. Whether extrinsic or intrinsic, these factors result in visible signs of skin damage. Typical skin damage includes thinning of the skin, which occurs naturally as one ages. With such thinning, there is a reduction in the cells and blood vessels that supply the skin as well as a flattening of the dermal-epidermal junction that results in weaker mechanical resistance of this junction. *See*, for example, Oikarinen, "The Aging of Skin: Chronoaging Versus Photoaging," *Photodermatol. Photoimmunol. Photomed.*, vol. 7, pp. 3-4, 1990. Other damages or changes seen in aging or damaged skin include fine lines, wrinkling, hyperpigmentation, sallowness, sagging, dark under-eye circles, puffy eyes, enlarged pores, diminished rate of turnover, and abnormal desquamation or exfoliation. Additional damage incurred as a result of both external and internal factors includes visible dead skin (i.e., flaking, scaling, dryness, roughness). Therefore, there is a need for products and methods that seek to remedy these keratinous tissue conditions.

Summary of the Invention

Without being limited by theory, it has been found that certain compositions containing a combination of N-acyl Phenylalanine or Tyrosine derivatives and an additional skin care active selected from sugar amines, vitamin B_3, retinoids, peptides, dialkanoyl hydroxyproline, hexamidine, salicylic acid, and phytosterol can prevent, retard, and/or treat uneven skin tone by acting as a lightening or pigmentation reduction cosmetic agent.

Consequently, Applicants have surprisingly found that topical compositions that contain specific N-acyl Phenylalanine or N-acyl Tyrosine or their derivatives in combination with at least one other skin care active selected from sugar amines, vitamin B_3, retinoids, peptides, dialkanoyl hydroxyproline, hexamidine, salicylic acid and phytosterol may be used to provide prophylactic as well as therapeutic treatments for keratinous tissue conditions. For instance, Applicants have found that such compositions may be useful for preventing, retarding, and/or treating uneven skin tone by acting as a lightening or pigmentation reduction cosmetic agent; preventing, retarding, and/or treating dark under-eye circles, puffy eyes, sagging, sallowness as well as spider vessels and/or red blotchiness of skin, promoting skin desquamation, exfoliation, and/or turnover, regulating and/or reducing pore size appearance, preventing/retarding tanning, regulating oily/shiny appearance, preventing, retarding, and/or treating hyperpigmentation (such as post-inflammatory hyperpigmentation, pigment spots such as age spots, and the like) in mammalian skin, preventing, retarding, and/or treating itchiness of mammalian skin, preventing, retarding, and/or treating dryness of skin, preventing, retarding, and/or treating fine lines and wrinkles, preventing, retarding, and/or treating skin atrophy of mammalian skin, and/or softening and/or smoothing lips, hair and nails of a mammal.

The present invention relates to a skin care composition comprising:

a) a safe and effective amount of an N-acyl amino acid selected from the group consisting of N-acyl Phenylalanine, N-acyl Tyrosine, their isomers, their salts, and derivatives thereof;

b) a safe and effective amount of at least one skin care active selected from the group consisting of sugar amines, vitamin B_3, retinoids, peptides, dialkanoyl hydroxyproline, hexamidine, salicylic acid, phytosterol, their derivatives, and combinations thereof; and

c) a dermatologically acceptable carrier for the N-acyl amino acid and the skin care active.

The invention further relates to methods for regulating the condition of mammalian keratinous tissue wherein the methods each comprise the step of topically applying to the

keratinous tissue of a mammal needing such treatment, a safe and effective amount of the skin care composition of the invention.

Detailed Description of the Invention

All percentages and ratios used herein are by weight of the total composition and all measurements made are at 25°C, unless otherwise designated.

The compositions of the present invention can comprise, consist essentially of, or consist of, the essential components as well as optional ingredients described herein. As used herein, "consisting essentially of" means that the composition or component may include additional ingredients, but only if the additional ingredients do not materially alter the basic and novel characteristics of the claimed compositions or methods.

The term "keratinous tissue," as used herein, refers to keratin-containing layers disposed as the outermost protective covering of mammals which includes, but is not limited to, skin, hair, toenails, fingernails, cuticles, hooves, etc.

The term "topical application", as used herein, means to apply or spread the compositions of the present invention onto the surface of the keratinous tissue.

The term "dermatologically acceptable," as used herein, means that the compositions or components described are suitable for use in contact with human keratinous tissue without undue toxicity, incompatibility, instability, allergic response, and the like.

The term "safe and effective amount" as used herein means an amount of a compound or composition sufficient to significantly induce a positive benefit, preferably a positive keratinous tissue appearance or feel benefit, including independently or in combination the benefits disclosed herein, but low enough to avoid serious side effects (i.e., to provide a reasonable benefit to risk ratio, within the scope of sound judgment of the skilled artisan).

The term "post-inflammatory hyperpigmentation" as used herein refers to the changes in melanin content as a response to an inflammatory event (e.g., acne, scratch, insect sting, sunburn, etc), especially in dark skin subjects.

The term "hyperpigmentation" as used herein refers to an area of skin wherein the pigmentation is greater than that of an adjacent area of skin (e.g., a pigment spot, an age spot, and the like).

The terms "desquamation, exfoliation, and/or turnover" as used herein mean the removal of the upper layers of the stratum corneum (comprising the horny layers).

The terms "oily and/or shiny appearance" as used herein mean the glossy look mammalian skin tends to exhibit upon the excretion of oil, sebum, and/or sweat from the respective source gland.

The term "sagging" as used herein means the laxity, slackness, or the like condition of skin that occurs as a result of loss of, damage to, alterations to, and/or abnormalities in dermal elastin.

The term "smoothing" and "softening" as used herein means altering the surface of the keratinous tissue such that its tactile feel is improved.

The term "sallowness" as used herein means the pale color, yellow color or the like condition of skin that occurs as a result of a loss of, damage to, alterations to, and/or abnormalities in skin components such that they become colored (e.g., yellow in color) due to processes such as protein glycation and accumulation of lipofuscin or in the decrease in peripheral blood flow that typically accompanies skin aging.

The compositions of the present invention are useful for topical application and for regulating keratinous tissue condition. Regulation of keratinous tissue condition, especially human skin condition, is often required due to conditions that may be induced or caused by factors internal and/or external to the body. For instance, "regulating skin condition" includes prophylactically regulating and/or therapeutically regulating skin condition, and may involve one or more of the following benefits: thickening (i.e., building the epidermis and/or dermis layers of the skin and/or the subcutaeous layers such as fat and muscle and where applicable the keratinous layers of the nail and hair shaft) to reduce atrophy (e.g., of the skin), increasing the convolution of the dermal-epidermal border, non-melanin skin discoloration such as under eye circles, blotching (e.g., uneven red coloration due to, e.g., rosacea) (hereinafter referred to as "red blotchiness"), sallowness (pale or yellow color), discoloration caused by telangiectasia or spider vessels, discolorations due to melanin (e.g., pigment spots, age spots, uneven pigmentation) and other chromophores in the skin (e.g., lipofuscin, protein crosslinks such as those that occur with glycation, and the like). As used herein, prophylactically regulating skin condition includes delaying, minimizing and/or preventing visible and/or tactile discontinuities in skin (e.g., texture irregularities, fine lines, wrinkles, sagging, stretch marks, cellulite, puffy eyes, and the like in the skin which may be detected visually or by feel). As used herein, therapeutically regulating skin condition includes ameliorating (e.g., diminishing, minimizing and/or effacing, discontinuities in skin. Regulating skin condition involves improving skin appearance and/or feel).

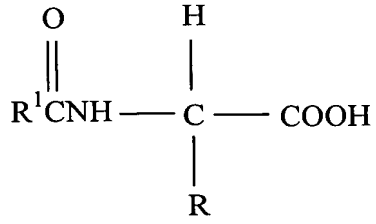
As used herein, "regulating skin condition" is intended to include regulation of such signs irrespective of the mechanism of origin.

The compositions of the present invention, including the essential and optional components thereof, are described in detail hereinafter.

Components

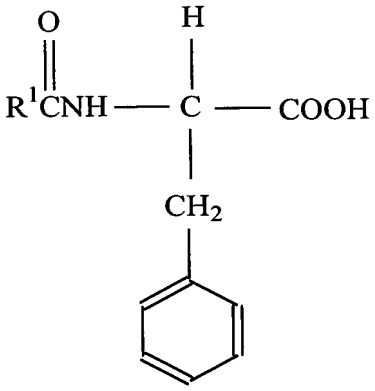
N-acyl Amino Acid Compound

The topical compositions of the present invention comprise a safe and effective amount of one or more N-acyl amino acid compounds. The amino acid can be one of any of the amino acids known in the art. The N-acyl amino acid compounds of the present invention correspond to the formula:



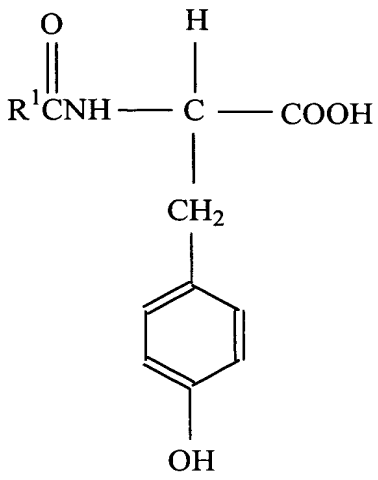
wherein R can be a hydrogen, alkyl (substituted or unsubstituted, branched or straight chain), or a combination of alkyl and aromatic groups. A list of possible side chains of amino acids known in the art are described in Stryer, Biochemistry, 1981, published by W.H. Freeman and Company. R^1 can be C_1 to C_{30}, saturated or unsaturated, straight or branched, substituted or unsubstituted alkyls; substituted or unsubstituted aromatic groups; or mixtures thereof.

Preferably, the N-acyl amino acid compound is selected from the group consisting of N-acyl Phenylalanine, N-acyl Tyrosine, their isomers, their salts, and derivatives thereof. The amino acid can be the D or L isomer or a mixture thereof. N-acyl Phenylalanine corresponds to the following formula:



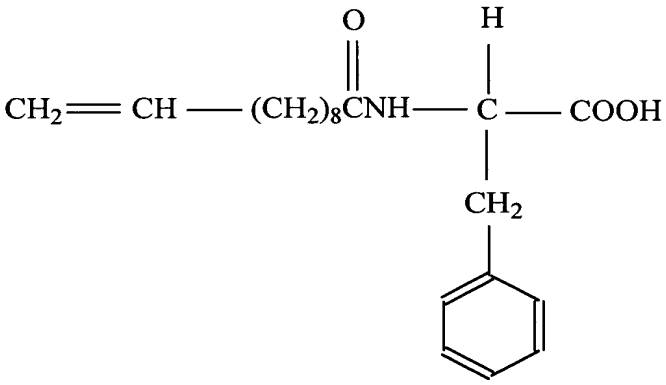
wherein R^1 can be C_1 to C_{30}, saturated or unsaturated, straight or branched, substituted or unsubstituted alkyls; substituted or unsubstituted aromatic groups; or mixtures thereof.

N-acyl Tyrosine corresponds to the following formula:



wherein R^1 can be C_1 to C_{30}, saturated or unsaturated, straight or branched, substituted or unsubstituted alkyls; substituted or unsubstituted aromatic groups; or mixtures thereof.

Particularly useful as a topical skin tone evening (lightening or pigmentation reduction) cosmetic agent is N-undecylenoyl-L-phenylalanine. This agent belongs to the broad class of N-acyl Phenylalanine derivatives, with its acyl group being a C11 mono-unsaturated fatty acid moiety and the amino acid being the L-isomer of phenylalanine. N-undecylenoyl-L-phenylalanine corresponds to the following formula:



As used herein, N-undecylenoyl-L-phenylalanine is commercially available under the tradename Sepiwhite® from SEPPIC.

In the composition of the present invention, the N-acyl amino acid preferably comprises from about 0.0001-25%, more preferably from about 0.001-10%, more preferably from about 0.01-5%, and even more preferably from about 0.02-2.5% by weight of the composition.

Skin Care Active

The present invention includes a skin care active that is selected from the group consisting of sugar amines, vitamin B_3, retinoids, peptides, dialkanoyl hydroxyproline, hexamidine, salicylic acid, phytosterol, their derivatives, and combinations thereof.

1. Sugar Amines (Amino Sugars)

The compositions of the present invention optionally include a safe and effective amount of a sugar amine, which are also known as amino sugars. The sugar amine compounds useful in the present invention are described in PCT Publication WO 02/076423 and US Patent No. 6,159,485.

Preferably, the composition contains from about 0.01% to about 15%, more preferably from about 0.1% to about 10%, and even more preferably from about 0.5% to about 5% by weight of the composition, of the sugar amine.

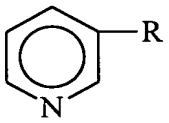
Sugar amines can be synthetic or natural in origin and can be used as pure compounds or mixtures of compounds (e.g., extracts from natural sources or mixtures of synthetic materials). Glucosamine is generally found in many shellfish and can also be derived from fungal sources. As used herein, "sugar amine" includes isomers and tautomers of such and its salts (e.g., HCl salt) and is commercially available from Sigma Chemical Co.

Examples of sugar amines that are useful herein include glucosamine, N-acetyl glucosamine, mannosamine, N-acetyl mannosamine, galactosamine, N-acetyl galactosamine, their isomers (e.g., stereoisomers), and their salts (e.g., HCl salt). Preferred for use herein are glucosamine, particularly D-glucosamine and N-acetyl glucosamine, particularly N-acetyl-D-glucosamine.

2. Vitamin B_3

The compositions of the present invention may include a safe and effective amount of a vitamin B_3 compound. Vitamin B_3 compounds are particularly useful for regulating skin condition as described in U.S. Patent No. 5,939,082. Preferably, the composition contains from about 0.01% to about 50%, more preferably from about 0.1% to about 20%, even more preferably from about 0.5% to about 10%, and still more preferably from about 1% to about 7%, even more preferably from about 2% to about 5%, by weight of the composition, of the vitamin B_3 compound.

As used herein, "vitamin B_3 compound" means a compound having the formula:



wherein R is - $CONH_2$ (i.e., niacinamide), - COOH (i.e., nicotinic acid) or - CH_2OH (i.e., nicotinyl alcohol); derivatives thereof; and salts of any of the foregoing.

Exemplary derivatives of the foregoing vitamin B_3 compounds include nicotinic acid esters, including non-vasodilating esters of nicotinic acid (e.g., tocopheryl nicotinate, myristyl nicotinate).

Examples of suitable vitamin B_3 compounds are well known in the art and are commercially available from a number of sources (e.g., the Sigma Chemical Company, ICN Biomedicals, Inc., and Aldrich Chemical Company).

3. Retinoid

The compositions of this invention may contain a safe and effective amount of a retinoid, such that the resultant composition is safe and effective for regulating keratinous tissue condition, preferably for regulating visible and/or tactile discontinuities in skin, more preferably for regulating signs of skin aging. The compositions preferably contain from about 0.001% to about 10%, more preferably from about 0.005% to about 2%, even more preferably from about 0.01% to about 1%, still more preferably from about 0.01% to about 0.5%, by weight of the composition, of the retinoid. The optimum concentration used in a composition will depend on the specific retinoid selected since their potency does vary considerably.

As used herein, "retinoid" includes all natural and/or synthetic analogs of Vitamin A or retinol-like compounds which possess the biological activity of Vitamin A in the skin as well as the geometric isomers and stereoisomers of these compounds. The retinoid is preferably selected from retinol, retinol esters (e.g., C_2 - C_{22} alkyl esters of retinol, including retinyl palmitate, retinyl acetate, retinyl propionate), retinal, and/or retinoic acid (including all-trans retinoic acid and/or 13-cis-retinoic acid), or mixtures thereof. More preferably the retinoid is a retinoid other than retinoic acid. Preferred retinoids are retinol, retinyl palmitate, retinyl acetate, retinyl propionate, retinal and combinations thereof. More preferred is retinyl propionate, used even more preferably from about 0.1% to about 0.3%.

4. Peptide

The compositions of the present invention may contain a safe and effective amount of a peptide, including but not limited to, di-, tri-, tetra-, penta-, and hexa-peptides and derivatives thereof. The compositions contain preferably from about $1x10^{-6}$% to about 20%, more preferably from about $1x10^{-6}$% to about 10%, even more preferably from about $1x10^{-5}$% to about 5%, by weight of the composition.

As used herein, "peptide" refers to peptides containing ten or fewer amino acids and their derivatives, isomers, and complexes with other species such as metal ions (e.g., copper, zinc,

manganese, magnesium, and the like). As used herein, peptide refers to both naturally occurring and synthesized peptides. Also useful herein are naturally occurring and commercially available compositions that contain peptides. More preferred peptides are the dipeptide carnosine (beta-ala-his), the tripeptide gly-his-lys, the pentapeptide lys-thr-thr-lys-ser, lipophilic derivatives of peptides, and metal complexes of the above, e.g., copper complex of the tripeptide his-gly-gly (also known as Iamin). A preferred commercially available tripeptide derivative-containing composition is Biopeptide CL®, which contains 100 ppm of palmitoyl-gly-his-lys and is commercially available from Sederma. A preferred commercially available pentapeptide derivative-containing composition is Matrixyl®, which contains 100 ppm of palmitoyl-lys-thr-thr-lys-ser and is commercially available from Sederma.

5. Phytosterol

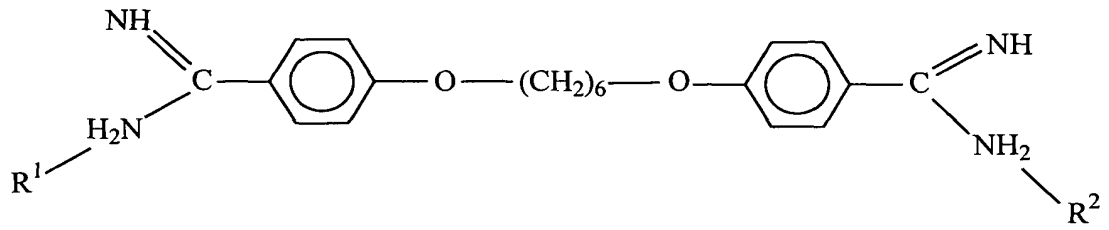
The topical compositions of the present invention comprise a safe and effective amount of one or more phytosterols selected from the group consisting of β-sitosterol, campesterol, brassicasterol, Δ5-avennasterol, lupenol, α-spinasterol, stigmasterol, their derivatives, analogs, and combinations thereof. More preferably, the phytosterol is selected from the group consisting of β-sitosterol, campesterol, brassicasterol, stigmasterol, their derivatives, and combinations thereof. More preferably, the phytosterol is stigmasterol.

Phytosterols can be synthetic or natural in origin and can be used as essentially pure compounds or mixtures of compounds (e.g., extracts from natural sources). Phytosterols are generally found in the unsaponifiable portion of vegetable oils and fats and are available as free sterols, acetylated derivatives, sterol esters, ethoxylated or glycosidic derivatives. More preferably, the phytosterols are free sterols. As used herein, "phytosterol" includes isomers and tautomers of such and is commercially available from Aldrich Chemical Company, Sigma Chemical Company, and Cognis.

In the compositions of the present invention, the phytosterol preferably comprises from about 0.0001% to about 25%, more preferably from about 0.001% to about 15%, even more preferably from about 0.01% to about 10%, still more preferably from about 0.1% to about 5%, and even more preferably from about 0.2% to about 2% by weight of the composition.

6. Hexamidine

The hexamidine compounds useful in the present invention correspond to those of the following chemical structure:



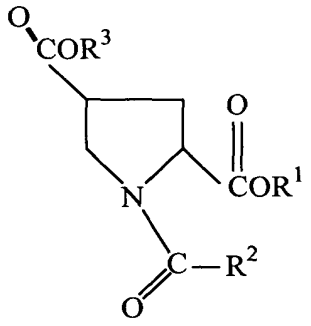
wherein R^1 and R^2 comprise organic acids (e.g., sulfonic acids, etc.).

In the composition of the present invention, the hexamidine preferably comprises from about 0.0001 to about 25%, more preferably from about 0.001 to about 10%, more preferably from about 0.01 to about 5%, and even more preferably from about 0.02 to about 2.5% by weight of the composition.

The topical compositions of the present invention optionally include a safe and effective amount of one or more of hexamidine compounds, its salts, and its derivatives. As used herein, hexamidine derivatives include any isomers and tautomers of hexamidine compounds including but not limited to organic acids and mineral acids, for example sulfonic acid, carboxylic acid etc. Preferably, the hexamidine compounds include hexamidine diisethionate, commercially available as Eleastab® HP100 from Laboratoires Serobiologiques.

7. Dialkanoyl Hydroxyproline Compounds

The dialkanoyl hydroxyproline compounds of the present invention correspond to those of the following chemical structure:



wherein R^1 comprises H, X, C_1-C_{20} straight or branched alkyl,

X comprises metals (Na, K, Li, Mg, Ca) or amines (DEA, TEA);

R^2 comprises C_1-C_{20} straight or branched alkyl;

R^3 comprises C_1-C_{20} straight or branched alkyl.

The topical compositions of the present invention may comprise a safe and effective amount of one or more dialkanoyl hydroxyproline compounds and their salts and derivatives. In

the composition of the present invention, the dialkanoyl hydroxyproline compounds preferably comprise from about 0.01 to 10%, more preferably from about 0. 1-5%, even more preferably from about 0.1 to 2% by weight of the composition

Suitable derivatives include but are not limited to esters, for example fatty esters, including, but not limited to tripalmitoyl hydroxyproline and dipalmityl acetyl hydroxyproline. A particularly useful compound is dipalmitoyl hydroxyproline. As used herein, dipalmitoyl hydroxyproline includes any isomers and tautomers of such and is commercially available under the tradename Sepilift DPHP® from Seppic, Inc. Further discussion of dipalmitoyl hydroxyproline appears in PCT Publication WO 93/23028. Preferably the dipalmitoyl hydroxyproline is the triethanolamine salt of dipalmitoyl hydroxyproline.

8. Salicylic Acid Compound

The topical compositions of the present invention may comprise a safe and effective amount of a salicylic acid compound, its esters, its salts, or combinations thereof. In the compositions of the present invention, the salicylic acid compound preferably comprises from about 0.0001% to about 25%, more preferably from about 0.001% to about 15%, even more preferably from about 0.01% to about 10%, still more preferably from about 0.1% to about 5%, and even more preferably from about 0.2% to about 2%, by weight of the composition, of salicylic acid.

Dermatologically Acceptable Carrier

The topical compositions of the present invention also comprise a dermatologically acceptable carrier for the N-acyl amino acids composition. The phrase "dermatologically acceptable carrier", as used herein, means that the carrier is suitable for topical application to the keratinous tissue, has good aesthetic properties, is compatible with the actives of the present invention and any other components, and will not cause any safety or toxicity concerns. A safe and effective amount of carrier is from about 50% to about 99.99%, preferably from about 60% to about 99.9%, more preferably from about 70% to about 98%, and even more preferably from about 80% to about 95% of the composition.

The carrier can be in a wide variety of forms. For example, emulsion carriers, including, but not limited to, oil-in-water, water-in-oil, water-in-oil-in-water, and oil-in-water-in-silicone emulsions, are useful herein.

Preferred carriers comprise an emulsion such as oil-in-water emulsions and water-in-oil emulsions, e.g., silicone-in-water or water-in-silicone emulsions. As will be understood by the skilled artisan, a given component will distribute primarily into either the water or oil phase, depending on the water solubility/dispensability of the component in the composition. Oil-in-water emulsions are especially preferred.

Emulsions according to the present invention generally contain a solution as described above and a lipid or oil. Lipids and oils may be derived from animals, plants, or petroleum and may be natural or synthetic (i.e., man-made). Preferred emulsions also contain a humectant, such as glycerin. Emulsions will preferably further contain from about 0.1% to about 10%, more preferably from about 0.2% to about 5%, of an emulsifier, based on the weight of the composition. Emulsifiers may be nonionic, anionic or cationic. Suitable emulsifiers are disclosed in, for example, U.S. Patent 3,755,560, U.S. Patent 4,421,769, and McCutcheon's Detergents and Emulsifiers, North American Edition, pages 317-324 (1986).

Suitable emulsions may have a wide range of viscosities, depending on the desired product form. Exemplary low viscosity emulsions, which are preferred, have a viscosity of about 50 centistokes or less, more preferably about 10 centistokes or less, even more preferably about 5 centistokes or less.

Preferred water-in-oil and oil-in-water emulsions are described in greater detail below.

1. Water-in-Oil emulsion

Water in oil emulsions are characterized as having a continuous hydrophobic, water insoluble oil phase and a water phase dispersed therein. The "oil phase" can contain oil, silicone or mixtures thereof. The distinction of whether the emulsion is characterized as a water-in-oil or water-in-silicone emulsion is a function of whether the oil phase is composed of primarily oil or silicone. A preferred example of a water-in-silicone emulsion is described below.

a. Continuous silicone phase

Preferred water-in-silicone emulsions of the present invention comprise from about 1% to about 60%, preferably from about 5% to about 40%, more preferably from about 10% to about 30%, by weight of a continuous silicone phase. The continuous silicone phase exists as an external phase that contains or surrounds the discontinuous aqueous phase described hereinafter.

The continuous silicone phase contains a silicone elastomer and/or polyorganosiloxane oil. The continuous silicone phase of these preferred emulsions comprises between about 50% and about 99.9% by weight of organopolysiloxane oil and less than about 50% by weight of a non-silicone oil. In a preferred embodiment, the continuous silicone phase comprises at least about 50%, preferably from about 60% to about 99.9%, more preferably from about 70% to about 99.9%, and even more preferably from about 80% to about 99.9%, polyorganosiloxane oil by weight of the continuous silicone phase, and up to about 50% non-silicone oils, preferably less about 40%, more preferably less than about 30%, even more preferably less than about 10%, and still more preferably less than about 2%, by weight of the continuous silicone phase.

b. Polyorganopolysiloxane Oil

The organopolysiloxane oil for use in the composition may be volatile, non-volatile, or a mixture of volatile and non-volatile silicones. The term "nonvolatile" as used in this context refers to those silicones that are liquid under ambient conditions and have a flash point (under one atmospheric of pressure) of or greater than about 100°C. The term "volatile" as used in this context refers to all other silicone oils. Suitable organopolysiloxanes can be selected from a wide variety of silicones spanning a broad range of volatilities and viscosities. Examples of suitable organopolysiloxane oils include polyalkylsiloxanes, cyclic polyalkylsiloxanes, and polyalkylarylsiloxanes.

Polyalkylsiloxanes useful in the composition herein include polyalkylsiloxanes with viscosities of from about 0.5 to about 1,000,000 centistokes at 25°C. Commercially available polyalkylsiloxanes include the polydimethylsiloxanes, which are also known as dimethicones, examples of which include the Vicasil® series sold by General Electric Company and the Dow Corning® 200 series sold by Dow Corning Corporation. Cyclic polyalkylsiloxanes suitable for use in the composition include those commercially available such as Dow Corning® 244, Dow Corning® 344 fluid, and Dow Corning® 345 fluid.

Also useful are materials such as trimethylsiloxysilicate, which is a polymeric material corresponding to the general chemical formula $[(CH_2)_3SiO_{1/2}]_x[SiO_2]y$, wherein x is an integer of from about 1 to about 500 and y is an integer of from about 1 to about 500. A commercially available trimethylsiloxysilicate is sold as a mixture with dimethicone as Dow Corning® 593 fluid.

Dimethiconols are also suitable for use in the composition. These compounds can be represented by the chemical formulas $R_3SiO[R_2SiO]_xSiR_2OH$ and $HOR_2SiO[R_2SiO]_xSiR_2OH$ wherein R is an alkyl group (preferably R is methyl or ethyl, more preferably methyl) and x is an integer of from 0 to about 500, chosen to achieve the desired molecular weight. Commercially available dimethiconols are typically sold as mixtures with dimethicone or cyclomethicone (e.g. Dow Corning® 1401, 1402, and 1403 fluids).

Polyalkylaryl siloxanes are also suitable for use in the composition. Polymethylphenyl siloxanes having viscosities of from about 15 to about 65 centistokes at 25°C are especially useful.

Preferred for use herein are organopolysiloxanes selected from the group consisting of polyalkylsiloxanes, alkyl substituted dimethicones, cyclomethicones, trimethylsiloxysilicates, dimethiconols, polyalkylaryl siloxanes, and mixtures thereof. More preferred for use herein are

polyalkylsiloxanes and cyclomethicones. Preferred among the polyalkylsiloxanes are dimethicones.

As stated above, the continuous silicone phase may contain one or more non-silicone oils. Suitable non-silicone oils have a melting point of about 25°C or less under about one atmosphere of pressure. Examples of non-silicone oils suitable for use in the continuous silicone phase are those well known in the chemical arts in topical personal care products in the form of water-in-oil emulsions, e.g., mineral oil, vegetable oils, synthetic oils, semisynthetic oils, etc.

c. Silicone Elastomer

The compositions of the present invention also include from about 0.1% to about 30%, by weight of the composition, of a silicone elastomer component. Preferably, the composition includes from about 1% to about 30%, more preferably from about 2% to about 20%, by weight of the composition, of the silicone elastomer component.

Suitable for use herein are silicone elastomers, which can be emulsifying or non-emulsifying crosslinked siloxane elastomers or mixtures thereof. No specific restriction exists as to the type of curable organopolysiloxane composition that can serve as starting material for the crosslinked organopolysiloxane elastomer. Examples in this respect are addition reaction-curing organopolysiloxane compositions which cure under platinum metal catalysis by the addition reaction between SiH-containing diorganopolysiloxane and organopolysiloxane having silicon-bonded vinyl groups; condensation-curing organopolysiloxane compositions which cure in the presence of an organotin compound by a dehydrogenation reaction between hydroxyl-terminated diorganopolysiloxane and SiH-containing diorganopolysiloxane and condensation-curing organopolysiloxane compositions which cure in the presence of an organotin compound or a titanate ester,

Addition reaction-curing organopolysiloxane compositions are preferred for their rapid curing rates and excellent uniformity of curing. A particularly preferred addition reaction-curing organopolysiloxane composition is prepared from:

(A) an organopolysiloxane having at least 2 lower alkenyl groups in each molecule;

(B) an organopolysiloxane having at least 2 silicon-bonded hydrogen atoms in each molecule; and

(C) a platinum-type catalyst.

The compositions of the present invention may include an emulsifying crosslinked organopolysiloxane elastomer, a non-emulsifying crosslinked organopolysiloxane elastomer, or a mixture thereof. The term "non-emulsifying," as used herein, defines crosslinked organopolysiloxane elastomers from which polyoxyalkylene units are absent. The term "emulsifying," as used herein, means crosslinked organopolysiloxane elastomers having at least

one polyoxyalkylene (e.g., polyoxyethylene or polyoxypropylene) unit. Preferred emulsifying elastomers herein include polyoxyalkylene modified elastomers formed from divinyl compounds, particularly siloxane polymers with at least two free vinyl groups, reacting with Si-H linkages on a polysiloxane backbone. Preferably, the elastomers are dimethyl polysiloxanes crosslinked by Si-H sites on a molecularly spherical MQ resin. Emulsifying crosslinked organopolysiloxane elastomers can notably be chosen from the crosslinked polymers described in US Patents 5,412,004, 5,837,793, and 5,811,487. In addition, an emulsifying elastomer comprised of dimethicone copolyol crosspolymer (and) dimethicone is available from Shin Etsu under the tradename KSG-21.

Advantageously, the non-emulsifying elastomers are dimethicone/vinyl dimethicone crosspolymers. Such dimethicone/vinyl dimethicone crosspolymers are supplied by a variety of suppliers including Dow Corning (DC 9040 and DC 9041), General Electric (SFE 839), Shin Etsu (KSG-15, 16, 18 [dimethicone/phenyl vinyl dimethicone crosspolymer]), and Grant Industries (GRANSIL™ line of elastomers). Cross-linked organopolysiloxane elastomers useful in the present invention and processes for making them are further described in U.S. Patent 4,970,252, U.S. Patent 5,760,116, and U.S. Patent 5,654,362. Additional crosslinked organopolysiloxane elastomers useful in the present invention are disclosed in Japanese Patent Application JP 61-18708, assigned to Pola Kasei Kogyo KK.

Commercially available elastomers preferred for use herein are Dow Corning's 9040 silicone elastomer blend, Shin Etsu's KSG-21, and mixtures thereof.

d. Carrier for Silicone Elastomer

The topical compositions of the present invention include from about 1% to about 80%, by weight of the composition, of a suitable carrier for the for the crosslinked organopolysiloxane elastomer component described above. The carrier, when combined with the cross-linked organopolysiloxane elastomer particles of the present invention, serves to suspend and swell the elastomer particles to provide an elastic, gel-like network or matrix. The carrier for the cross-linked siloxane elastomer is liquid under ambient conditions, and preferably has a low viscosity to provide for improved spreading on the skin.

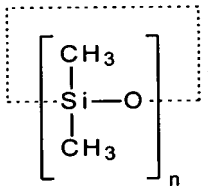
Concentrations of the carrier in the cosmetic compositions of the present invention will vary primarily with the type and amount of carrier and the cross-linked siloxane elastomer employed. Preferred concentrations of the carrier are from about 5% to about 50%, more preferably from about 5% to about 40%, by weight of the composition.

The carrier for the cross-linked siloxane elastomer includes one or more liquid carriers suitable for topical application to human skin. These liquid carriers may be organic, silicone-containing or fluorine-containing, volatile or non-volatile, polar or non-polar, provided that the

liquid carrier forms a solution or other homogenous liquid or liquid dispersion with the selected cross-linked siloxane elastomer at the selected siloxane elastomer concentration at a temperature of from about 28° C. to about 250° C., preferably from about 28° C. to about 100° C., preferably from about 28° C. to about 78° C. The term "volatile" as used herein refers to all materials that are not "non-volatile" as previously defined herein. The phrase "relatively polar" as used herein means more polar than another material in terms of solubility parameter; i.e., the higher the solubility parameter the more polar the liquid. The term "non-polar" typically means that the material has a solubility parameter below about 6.5 $(cal/cm^3)^{0.5}$.

e. Non-polar, Volatile Oils

The non-polar, volatile oil tends to impart highly desirable aesthetic properties to the compositions of the present invention. Consequently, the non-polar, volatile oils are preferably utilized at a fairly high level. Non-polar, volatile oils particularly useful in the present invention are silicone oils; hydrocarbons; and mixtures thereof. Such non-polar, volatile oils are disclosed, for example, in Cosmetics, Science, and Technology, Vol. 1, 27-104 edited by Balsam and Sagarin, 1972. Examples of preferred non-polar, volatile hydrocarbons include polydecanes such as isododecane and isodecane (e.g., Permethyl-99A which is available from Presperse Inc.) and the C7 -C8 through C12 -C15 isoparaffins (such as the Isopar Series available from Exxon Chemicals). Particularly preferred volatile silicone oils are selected from cyclic volatile silicones corresponding to the formula:



wherein n is from about 3 to about 7; and linear volatile silicones corresponding to the formula:

$$(CH_3)_3\ Si\text{--}O\text{--}[Si(CH_3)_2\text{-}O]_m\ \text{--}Si(CH_3)_3$$

wherein m is from about 1 to about 7. Linear volatile silicones generally have a viscosity of less than about 5 centistokes at 25° C., whereas the cyclic silicones have viscosities of less than about 10 centistokes at 25° C. Highly preferred examples of volatile silicone oils include cyclomethicones of varying viscosities, e.g., Dow Corning 200, Dow Corning 244, Dow Corning 245, Dow Corning 344, and Dow Corning 345, (commercially available from Dow Corning Corp.); SF-1204 and SF-1202 Silicone Fluids (commercially available from G.E. Silicones), GE 7207 and 7158 (commercially available from General Electric Co.); and SWS-03314 (commercially available from SWS Silicones Corp.).

f. Relatively Polar, Non-volatile oils

The non-volatile oil is "relatively polar" as compared to the non-polar, volatile oil discussed above. Therefore, the non-volatile co-carrier is more polar (i.e., has a higher solubility parameter) than at least one of the non-polar, volatile oils. Relatively polar, non-volatile oils potentially useful in the present invention are disclosed, for example, in Cosmetics, Science, and Technology, Vol. 1, 27-104 edited by Balsam and Sagarin, 1972; U.S. Patents 4,202,879 and 4,816,261. Relatively polar, non-volatile oils useful in the present invention are preferably selected from silicone oils; hydrocarbon oils; fatty alcohols; fatty acids; esters of mono and dibasic carboxylic acids with mono and polyhydric alcohols; polyoxyethylenes; polyoxypropylenes; mixtures of polyoxyethylene and polyoxypropylene ethers of fatty alcohols; and mixtures thereof.

g. Non-polar, Non-volatile oils

In addition to the liquids discussed above, the carrier for the cross-linked siloxane elastomer may optionally include non-volatile, non-polar oils. Typical non-volatile, non-polar emollients are disclosed, for example, in Cosmetics, Science, and Technology, Vol. 1, 27-104 edited by Balsam and Sagarin, 1972; U.S. Patents 4,202,879 and 4,816,261. The non-volatile oils useful in the present invention are essentially non-volatile polysiloxanes, paraffinic hydrocarbon oils, and mixtures thereof.

h. Dispersed aqueous phase

The topical compositions of the present invention comprise from about 30% to about 90%, more preferably from about 50% to about 85%, and even more preferably from about 70% to about 80% of a dispersed aqueous phase. In emulsion technology, the term "dispersed phase" is a term well-known to one skilled in the art which means that the phase exists as small particles or droplets that are suspended in and surrounded by a continuous phase. The dispersed phase is also known as the internal or discontinuous phase. The dispersed aqueous phase is a dispersion of small aqueous particles or droplets suspended in and surrounded by the continuous silicone phase described hereinbefore.

The aqueous phase can be water, or a combination of water and one or more water soluble or dispersible ingredients. Nonlimiting examples of such optional ingredients include thickeners, acids, bases, salts, chelants, gums, water-soluble or dispersible alcohols and polyols, buffers, preservatives, sunscreening agents, colorings, and the like.

The topical compositions of the present invention will typically comprise from about 25% to about 90%, preferably from about 40% to about 85%, more preferably from about 60% to about 80%, water in the dispersed aqueous phase by weight of the composition.

i. Emulsifier for dispersing the aqueous phase

The water-in-silicone emulsions of the present invention preferably comprise an emulsifier. In a preferred embodiment, the composition contains from about 0.1% to about 10% emulsifier, more preferably from about 0.2% to about 7.5%, even more preferably from about 0.5% to about 5%, emulsifier by weight of the composition. The emulsifier helps disperse and suspend the aqueous phase within the continuous silicone phase.

A wide variety of emulsifying agents can be employed herein to form the preferred water-in-silicone emulsion. Known or conventional emulsifying agents can be used in the composition, provided that the selected emulsifying agent is chemically and physically compatible with essential components of the composition, and provides the desired dispersion characteristics. Suitable emulsifiers include silicone emulsifiers, non-silicon-containing emulsifiers, and mixtures thereof, known by those skilled in the art for use in topical personal care products. Preferably these emulsifiers have an HLB value of less than about 14, more preferably from about 2 to about 14, and even more preferably from about 4 to about 14. Emulsifiers having an HLB value outside of these ranges can be used in combination with other emulsifiers to achieve an effective weighted average HLB for the combination that falls within these ranges.

Silicone emulsifiers are preferred. A wide variety of silicone emulsifiers are useful herein. These silicone emulsifiers are typically organically modified organopolysiloxanes, also known to those skilled in the art as silicone surfactants. Useful silicone emulsifiers include dimethicone copolyols.

Nonlimiting examples of dimethicone copolyols and other silicone surfactants useful as emulsifiers herein include polydimethylsiloxane polyether copolymers with pendant polyethylene oxide side chains, polydimethylsiloxane polyether copolymers with pendant polypropylene oxide side chains, polydimethylsiloxane polyether copolymers with pendant mixed polyethylene oxide and polypropylene oxide side chains, polydimethylsiloxane polyether copolymers with pendant mixed poly(ethylene)(propylene)oxide side chains, polydimethylsiloxane polyether copolymers with pendant organobetaine side chains, polydimethylsiloxane polyether copolymers with pendant carboxylate side chains, polydimethylsiloxane polyether copolymers with pendant quaternary ammonium side chains; and also further modifications of the preceding copolymers containing pendant C2-C30 straight, branched, or cyclic alkyl moieties. Examples of commercially available dimethicone copolyols useful herein sold by Dow Corning Corporation are Dow Corning® 190, 193, Q2-5220, 2501 Wax, 2-5324 fluid, and 3225C (this latter material being sold as a mixture with cyclomethicone). Cetyl dimethicone copolyol is commercially available as a mixture with polyglyceryl-4 isostearate (and) hexyl laurate and is sold under the tradename ABIL® WE-09 (available from Goldschmidt). Cetyl dimethicone copolyol is also commercially available as a

mixture with hexyl laurate (and) polyglyceryl-3 oleate (and) cetyl dimethicone and is sold under the tradename ABIL® WS-08 (also available from Goldschmidt). Other nonlimiting examples of dimethicone copolyols also include lauryl dimethicone copolyol, dimethicone copolyol acetate, diemethicone copolyol adipate, dimethicone copolyolamine, dimethicone copolyol behenate, dimethicone copolyol butyl ether, dimethicone copolyol hydroxy stearate, dimethicone copolyol isostearate, dimethicone copolyol laurate, dimethicone copolyol methyl ether, dimethicone copolyol phosphate, and dimethicone copolyol stearate.

Among the non-silicone-containing emulsifiers useful herein are various non-ionic and anionic emulsifying agents such as sugar esters and polyesters, alkoxylated sugar esters and polyesters, C1-C30 fatty acid esters of C1-C30 fatty alcohols, alkoxylated derivatives of C1-C30 fatty acid esters of C1-C30 fatty alcohols, alkoxylated ethers of C1-C30 fatty alcohols, polyglyceryl esters of C1-C30 fatty acids, C1-C30 esters of polyols, C1-C30 ethers of polyols, alkyl phosphates, polyoxyalkylene fatty ether phosphates, fatty acid amides, acyl lactylates, soaps, and mixtures thereof. Other suitable emulsifiers are described, for example, in McCutcheon's, Detergents and Emulsifiers, North American Edition (1986), published by Allured Publishing Corporation; U.S. Patent Nos. 5,011,681, 4,421,769, and 3,755,560.

2. Oil-in-Water Emulsions

Other preferred topical carriers include oil-in-water emulsions, having a continuous aqueous phase and a hydrophobic, water-insoluble phase ("oil phase") dispersed therein. The "oil phase" can contain oil, silicone or mixtures thereof, and includes but is not limited to the oils and silicones described above in the section on water-in-oil emulsions. The distinction of whether the emulsion is characterized as an oil-in-water or silicone-in-water emulsions is a function of whether the oil phase is composed of primarily oil or silicone. The water phase of these emulsions consists primarily of water, but can also contain various other ingredients such as those water phase ingredients listed in the above section on water-in-oil emulsion. The preferred oil-in-water emulsions comprises from about 25% to about 98%, preferably from about 65% to about 95%, more preferably from about 70% to about 90% water by weight of the total composition.

In addition to a continuous water phase and dispersed oil or silicone phase, these oil-in-water compositions also comprise an emulsifier to stabilize the emulsion. Emulsifiers useful herein are well known in the art, and include nonionic, anionic, cationic, and amphoteric emulsifiers. Non-limiting examples of emulsifiers useful in the oil-in-water emulsions of this invention are given in McCutcheon's, Detergents and Emulsifiers, North American Edition (1986), published by Allured Publishing Corporation; U.S. Patent 5,011,681; U.S. Patent 4,421,769; and U.S. Patent 3,755,560.

Optional Components

The compositions of the present invention may contain a variety of other ingredients that are conventionally used in given product types provided that they do not unacceptably alter the benefits of the invention.

The optional components, when incorporated into the composition, should be suitable for use in contact with human keratinous tissue without undue toxicity, incompatibility, instability, allergic response, and the like within the scope of sound judgment. The *CTFA Cosmetic Ingredient Handbook*, Second Edition (1992) describes a wide variety of nonlimiting cosmetic and pharmaceutical ingredients commonly used in the skin care industry, which are suitable for use in the compositions of the present invention. Examples of these ingredient classes include: abrasives, absorbents, aesthetic components such as fragrances, pigments, colorings/colorants, essential oils, skin sensates, astringents, etc. (e.g., clove oil, menthol, camphor, eucalyptus oil, eugenol, menthyl lactate, witch hazel distillate), anti-acne agents, anti-caking agents, antifoaming agents, antimicrobial agents (e.g., iodopropyl butylcarbamate), antioxidants, binders, biological additives, buffering agents, bulking agents, chelating agents, chemical additives, colorants, cosmetic astringents, cosmetic biocides, denaturants, drug astringents, external analgesics, film formers or materials, e.g., polymers, for aiding the film-forming properties and substantivity of the composition (e.g., copolymer of eicosene and vinyl pyrrolidone), opacifying agents, pH adjusters, propellants, reducing agents, sequestrants, skin bleaching and lightening agents, skin-conditioning agents, skin soothing and/or healing agents and derivatives, skin treating agents, thickeners, and vitamins and derivatives thereof.

In any embodiment of the present invention, however, the actives useful herein can be categorized by the benefit they provide or by their postulated mode of action. However, it is to be understood that the actives useful herein can in some instances provide more than one benefit or operate via more than one mode of action. Therefore, classifications herein are made for the sake of convenience and are not intended to limit the active to that particular application or applications listed.

1. Desquamation Actives

A safe and effective amount of a desquamation active may be added to the compositions of the present invention, more preferably from about 0.01% to about 10%, even more preferably from about 0.5% to about 5%, also preferably from about 0.1% to about 2%, by weight of the composition. Desquamation actives enhance the skin appearance benefits of the present invention. For example, the desquamation actives tend to improve the texture of the skin (e.g., smoothness). One desquamation system that is suitable for use herein comprises salicylic acid and zwitterionic surfactants and is described in U.S. Patent No. 5,652,228. Zwitterionic

surfactants such as described in these applications are also useful as desquamatory agents herein, with cetyl betaine being particularly preferred.

2. Anti-Acne Actives

The compositions of the present invention may comprise a safe and effective amount of one or more anti-acne actives. Examples of useful anti-acne actives include resorcinol, sulfur, erythromycin, zinc, dehydroacetic acid, etc. Further examples of suitable anti-acne actives are described in further detail in U. S. Patent No. 5,607,980.

3. Anti-Wrinkle Actives/Anti-Atrophy Actives

The compositions of the present invention may further comprise a safe and effective amount of one or more anti-wrinkle actives or anti-atrophy actives. Exemplary anti-wrinkle/anti-atrophy actives suitable for use in the compositions of the present invention include hydroxy acids (e.g., salicylic acid, glycolic acid), keto acids (e.g., pyruvic acid), ascorbic acid (vitamin C), phytic acid, lysophosphatidic acid, flavonoids (e.g., isoflavones, flavones, etc.), stilbenes, cinnamates, resveratrol, kinetin, zeatin, dimethylaminoethanol, peptides from natural sources (e.g., soy peptides), salts of sugar acids (e.g., Mn gluconate), and retinoids which enhance the keratinous tissue appearance benefits of the present invention, especially in regulating keratinous tissue condition, e.g., skin condition, and other vitamin B compounds (e.g., thiamine (vitamin B1), pantothenic acid (vitamin B5), carnitine (vitamin Bt), riboflavin (vitamin B2), and their derivatives and salts (e.g., HCl salts or calcium salts)).

4. Anti-Oxidants/Racial Scavengers

The compositions of the present invention may include a safe and effective amount of an anti-oxidant/radical scavenger. The anti-oxidant/radical scavenger is especially useful for providing protection against UV radiation that can cause increased scaling or texture changes in the stratum corneum and against other environmental agents, which can cause skin damage.

A safe and effective amount of an anti-oxidant/radical scavenger may be added to the compositions of the subject invention, preferably from about 0.01% to about 10%, more preferably from about 0.1% to about 5%, of the composition.

Anti-oxidants/radical scavengers such as ascorbic acid (vitamin C) and its salts, ascorbyl esters of fatty acids, ascorbic acid derivatives (e.g., magnesium ascorbyl phosphate), tocopherol (vitamin E), tocopherol sorbate, tocopherol acetate, other esters of tocopherol, butylated hydroxy benzoic acids and their salts, 6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid (commercially available under the tradename Trolox^{R}), amines (e.g., N,N-diethylhydroxylamine, amino-guanidine), nordihydroguaiaretic acid, bioflavonoids, amino acidssilymarin, tea extracts, and grape skin/seed extracts may be used. Preferred anti-oxidants/radical scavengers are selected from esters of tocopherol, more preferably tocopherol acetate.

5. Chelators

The compositions of the present invention may also comprise a safe and effective amount of a chelator or chelating agent. As used herein, "chelator" or "chelating agent" means an active agent capable of removing a metal ion from a system by forming a complex so that the metal ion cannot readily participate in or catalyze oxygen radical formation. The inclusion of a chelating agent is especially useful for providing protection against UV radiation that can contribute to skin damage.

A safe and effective amount of a chelating agent may be added to the compositions of the subject invention, preferably from about 0.1% to about 10%, more preferably from about 1% to about 5%, of the composition. Exemplary chelators that are useful herein are disclosed in U.S. Patent No. 5,487,884. Preferred chelators useful in compositions of the subject invention are furildioxime and derivatives thereof.

6. Flavonoids

The compositions of the present invention may optionally comprise a flavonoid compound. Flavonoids are broadly disclosed in U.S. Patents 5,686,082 and 5,686,367. Examples of flavonoids particularly suitable for use in the present invention are one or more flavones, one or more isoflavones, one or more coumarins, one or more chromones, one or more dicoumarols, one or more chromanones, one or more chromanols, isomers (e.g., cis/trans isomers) thereof, and mixtures thereof.

Preferred for use herein are flavones and isoflavones, in particular daidzein (7,4'-dihydroxy isoflavone), genistein (5,7,4'-trihydroxy isoflavone), equol (7,4'-dihydroxy isoflavan), 5,7-dihydroxy-4'-methoxy isoflavone, soy isoflavones (a mixture extracted from soy), and mixtures thereof.

Flavonoid compounds useful herein are commercially available from a number of sources, e.g., Indofine Chemical Company, Inc., Steraloids, Inc., and Aldrich Chemical Company, Inc.

The herein described flavonoid compounds are preferably present in the instant invention at concentrations of from about 0.01% to about 20%, more preferably from about 0.1% to about 10%, and even more preferably from about 0.5% to about 5%.

7. Anti-Inflammatory Agents

A safe and effective amount of an anti-inflammatory agent may be added to the compositions of the present invention, preferably from about 0.01% to about 10%, more preferably from about 0.5% to about 5%, of the composition. The anti-inflammatory agent enhances the skin appearance benefits of the present invention, e.g., such agents contribute to a more uniform and acceptable skin tone or color. The exact amount of anti-inflammatory agent to

be used in the compositions will depend on the particular anti-inflammatory agent utilized since such agents vary widely in potency.

Steroidal anti-inflammatory agents, include but are not limited to, corticosteroids such as hydrocortisone. A second class of anti-inflammatory agents, which is useful in the compositions, includes the nonsteroidal anti-inflammatory agents. The varieties of compounds encompassed by this group are well known to those skilled in the art. Specific non-steroidal anti-inflammatory agents useful in the composition invention include, but are not limited to, salicylates, flufenamic acid, etofenamate, aspirin, and mixtures thereof.

Additional anti-inflammatory agents useful herein include allantoin and compounds of the Licorice (the plant genus/species Glycyrrhiza glabra) family, including glycyrrhetic acid, glycyrrhizic acid, and derivatives thereof (e.g., salts and esters).

8. Anti-Cellulite Agents

The compositions of the present invention may also comprise a safe and effective amount of an anti-cellulite agent. Suitable agents may include, but are not limited to, xanthine compounds (e.g., caffeine, theophylline, theobromine, and aminophylline).

9. Tanning Actives

The compositions of the present invention may comprise a tanning active. When present, it is preferable that the compositions comprise from about 0.1% to about 20%, more preferably from about 2% to about 7%, and even more preferably from about 3% to about 6%, by weight of the composition, of a tanning active. A preferred tanning active is dihydroxyacetone.

10. Skin Lightening Agents

The compositions of the present invention may comprise a skin lightening agent. When used, the compositions preferably comprise from about 0.1% to about 10%, more preferably from about 0.2% to about 5%, also preferably from about 0.5% to about 2%, by weight of the composition, of a skin lightening agent. Suitable skin lightening agents include those known in the art, including kojic acid, arbutin, tranexamic acid, ascorbic acid and derivatives thereof (e.g., magnesium ascorbyl phosphate or sodium ascorbyl phosphate, ascorbyl glucoside, and the like). Other skin lightening materials suitable for use herein include Acitwhite ® (Cognis), Emblica ® (Rona), Azeloglicina (Sinerga) and extracts (e.g. mulberry extract).

11. Antimicrobial and Antifungal Actives

The compositions of the present invention may comprise an antimicrobial or antifungal active. Such actives are capable of destroying microbes, preventing the development of microbes or preventing the pathogenic action of microbes. A safe and effective amount of an antimicrobial or antifungal active may be added to the present compositions, preferably, from about 0.001% to

about 10%, more preferably from about 0.01% to about 5%, and even more preferably from about 0.05% to about 2% by weight of the composition.

Preferred examples of actives useful herein include those selected from the group consisting of salicylic acid, benzoyl peroxide, 3-hydroxy benzoic acid, glycolic acid, lactic acid, 4-hydroxy benzoic acid, acetyl salicylic acid, 2-hydroxybutanoic acid, 2-hydroxypentanoic acid, 2-hydroxyhexanoic acid, cis-retinoic acid, trans-retinoic acid, retinol, phytic acid, N-acetyl-L-cysteine, lipoic acid, azelaic acid, arachidonic acid, benzoylperoxide, tetracycline, ibuprofen, naproxen, hydrocortisone, acetominophen, resorcinol, phenoxyethanol, phenoxypropanol, phenoxyisopropanol, 2,4,4'-trichloro-2'-hydroxy diphenyl ether, 3,4,4'-trichlorocarbanilide, octopirox, ciclopirox, lidocaine hydrochloride, clotrimazole, miconazole, ketoconazole, neocycin sulfate, and mixtures thereof.

12. Sunscreen Actives

The compositions of the subject invention may optionally contain a sunscreen active. As used herein, "sunscreen active" includes both sunscreen agents and physical sunblocks. Suitable sunscreen actives may be organic or inorganic.

A wide variety of conventional sunscreen actives are suitable for use herein. Sagarin, et al., at Chapter VIII, pages 189 et seq., of Cosmetics Science and Technology (1972), discloses numerous suitable actives. Particularly suitable sunscreen agents are 2-ethylhexyl-p-methoxycinnamate (commercially available as PARSOL MCX), 4,4'-t-butyl methoxydibenzoyl-methane (commercially available as PARSOL 1789), 2-hydroxy-4-methoxybenzophenone, octyldimethyl-p-aminobenzoic acid, digalloyltrioleate, 2,2-dihydroxy-4-methoxybenzophenone, ethyl-4-(bis(hydroxy-propyl))aminobenzoate, 2-ethylhexyl-2-cyano-3,3-diphenylacrylate, 2-ethylhexyl-salicylate, glyceryl-p-aminobenzoate, 3,3,5-tri-methylcyclohexylsalicylate, methylanthranilate, p-dimethyl-aminobenzoic acid or aminobenzoate, 2-ethylhexyl-p-dimethyl-amino-benzoate, 2-phenylbenzimidazole-5-sulfonic acid, 2-(p-dimethylaminophenyl)-5-sulfonicbenzoxazoic acid, octocrylene, zinc oxide, titanium dioxide, and mixtures of these compounds.

Preferred organic sunscreen actives useful in the compositions useful in the subject invention are 2-ethylhexyl-p-methoxycinnamate, butylmethoxydibenzoyl-methane, 2-hydroxy-4-methoxybenzo-phenone, 2-phenylbenzimidazole-5-sulfonic acid, octyldimethyl-p-aminobenzoic acid, octocrylene, zinc oxide, titanium dioxide, and mixtures thereof. Especially preferred sunscreen actives include 4,4'-t-butylmethoxydibenzoylmethane, 2-ethylhexyl-p-methoxycinnamate, phenyl benzimidazole sulfonic acid, octocrylene, zinc oxide, and titanium dioxide, and mixtures thereof.

A safe and effective amount of the sunscreen active is used, typically from about 1% to about 20%, more typically from about 2% to about 10% by weight of the composition. Exact amounts will vary depending upon the sunscreen chosen and the desired Sun Protection Factor (SPF).

13. Conditioning Agents

The compositions of the present invention may comprise a conditioning agent selected from the group consisting of humectants, moisturizers, or skin conditioners. A variety of these materials can be employed and each can be present at a level of from about 0.01% to about 40%, more preferably from about 0.1% to about 30%, and even more preferably from about 0.5% to about 15% by weight of the composition. These materials include, but are not limited to, guanidine; urea; glycolic acid and glycolate salts (e.g. ammonium and quaternary alkyl ammonium); lactic acid and lactate salts (e.g., ammonium and quaternary alkyl ammonium); aloe vera in any of its variety of forms (e.g., aloe vera gel); polyhydroxy compounds such as sorbitol, mannitol, glycerol, hexanetriol, butanetriol, propylene glycol, butylene glycol, hexylene glycol and the like; polyethylene glycols; sugars (e.g., melibiose) and starches; sugar and starch derivatives (e.g., alkoxylated glucose, fructose, sucrose, etc.); hyaluronic acid; lactamide monoethanolamine; acetamide monoethanolamine; sucrose polyester; petrolatum; and mixtures thereof.

Preferably, the conditioning agent is selected from the group consisting of glycerol, urea, petrolatum, sucrose polyester, and combinations thereof.

14. Thickening Agents (including thickeners and gelling agents)

The compositions of the present invention can comprise one or more thickening agents, preferably from about 0.05% to about 10%, more preferably from about 0.1% to about 5%, and even more preferably from about 0.25% to about 4%, by weight of the composition.

Nonlimiting classes of thickening agents include those selected from the group consisting of:

a. Carboxylic Acid Polymers

These polymers are crosslinked compounds containing one or more monomers derived from acrylic acid, substituted acrylic acids, and salts and esters of these acrylic acids and the substituted acrylic acids, wherein the crosslinking agent contains two or more carbon-carbon double bonds and is derived from a polyhydric alcohol.

Examples of commercially available carboxylic acid polymers useful herein include the carbomers, which are homopolymers of acrylic acid crosslinked with allyl ethers of sucrose or pentaerytritol. The carbomers are available as the Carbopol® 900 series from B.F. Goodrich

(e.g., Carbopol® 954). In addition, other suitable carboxylic acid polymeric agents include copolymers of C_{10-30} alkyl acrylates with one or more monomers of acrylic acid, methacrylic acid, or one of their short chain (i.e., C_{1-4} alcohol) esters, wherein the crosslinking agent is an allyl ether of sucrose or pentaerytritol. These copolymers are known as acrylates/C_{10-30} alkyl acrylate crosspolymers and are commercially available as Carbopol® 1342, Carbopol® 1382, Pemulen TR-1, and Pemulen TR-2, from B.F. Goodrich. In other words, examples of carboxylic acid polymer thickeners useful herein are those selected from the group consisting of carbomers, acrylates/C_{10}-C_{30} alkyl acrylate crosspolymers, and mixtures thereof.

b. Crosslinked Polyacrylate Polymers

The compositions of the present invention can optionally comprise crosslinked polyacrylate polymers useful as thickeners or gelling agents including both cationic and nonionic polymers, with the cationics being generally preferred. Examples of useful crosslinked nonionic polyacrylate polymers and crosslinked cationic polyacrylate polymers are those described in U. S. Patent No. 5,100,660, U. S. Patent No. 4,849,484, U. S. Patent No. 4,835,206, U.S. Patent No. 4,628,078, U.S. Patent No. 4,599,379, and EP 228,868.

c. Polyacrylamide Polymers

The compositions of the present invention can optionally comprise polyacrylamide polymers, especially nonionic polyacrylamide polymers including substituted branched or unbranched polymers. Preferred among these polyacrylamide polymers is the nonionic polymer given the CTFA designation polyacrylamide and isoparaffin and laureth-7, available under the Tradename Sepigel 305 from Seppic Corporation.

Other polyacrylamide polymers useful herein include multi-block copolymers of acrylamides and substituted acrylamides with acrylic acids and substituted acrylic acids. Commercially available examples of these multi-block copolymers include Hypan SR150H, SS500V, SS500W, SSSA100H, from Lipo Chemicals, Inc.

d. Polysaccharides

A wide variety of polysaccharides are useful herein. "Polysaccharides" refer to gelling agents that contain a backbone of repeating sugar (i.e., carbohydrate) units. Nonlimiting examples of polysaccharide gelling agents include those selected from the group consisting of cellulose, carboxymethyl hydroxyethylcellulose, cellulose acetate propionate carboxylate, hydroxyethylcellulose, hydroxyethyl ethylcellulose, hydroxypropylcellulose, hydroxypropyl methylcellulose, methyl hydroxyethylcellulose, microcrystalline cellulose, sodium cellulose sulfate, and mixtures thereof. Also useful herein are the alkyl-substituted celluloses. Preferred among the alkyl hydroxyalkyl cellulose ethers is the material given the CTFA designation cetyl

hydroxyethylcellulose, which is the ether of cetyl alcohol and hydroxyethylcellulose. This material is sold under the tradename Natrosol® CS Plus from Aqualon Corporation.

Other useful polysaccharides include scleroglucans comprising a linear chain of (1-3) linked glucose units with a (1-6) linked glucose every three units, a commercially available example of which is Clearogel™ CS11 from Michel Mercier Products Inc.

e. Gums

Other thickening and gelling agents useful herein include materials that are primarily derived from natural sources. Nonlimiting examples of these gelling agent gums include materials selected from the group consisting of acacia, agar, algin, alginic acid, ammonium alginate, amylopectin, calcium alginate, calcium carrageenan, carnitine, carrageenan, dextrin, gelatin, gellan gum, guar gum, guar hydroxypropyltrimonium chloride, hectorite, hyaluroinic acid, hydrated silica, hydroxypropyl chitosan, hydroxypropyl guar, karaya gum, kelp, locust bean gum, natto gum, potassium alginate, potassium carrageenan, propylene glycol alginate, sclerotium gum, sodium carboyxmethyl dextran, sodium carrageenan, tragacanth gum, xanthan gum, and mixtures thereof.

15. Water-Soluble Vitamins

The compositions of the present invention may contain a safe and effective amount of one or more water-soluble vitamins. Examples of water-soluble vitamins include, but are not limited to, water-soluble versions of vitamin B, vitamin B derivatives, vitamin C, vitamin C derivatives, vitamin K, vitamin K derivatives, vitamin D, vitamin D derivatives, vitamin E, vitamin E derivatives, and mixtures thereof. The vitamin compounds may be included as the substantially pure material, or as an extract obtained by suitable physical and/or chemical isolation from natural (e.g., plant) sources. When vitamin compounds are present in the compositions of the instant invention, the compositions preferably contain from about 0.0001% to about 50%, more preferably from about 0.001% to about 10%, still more preferably from about 0.01% to about 5%, and still more preferably from about 0.1% to about 5%, by weight of the composition, of the vitamin compound.

16. Particulate Material

The compositions of the present invention may contain one or more particulate materials. Nonlimiting examples of particulate materials useful in the present invention include colored and uncolored pigments, interference pigments, inorganic powders, organic powders, composite powders, optical brightener particles, and combinations thereof. These particulates can be platelet shaped, spherical, elongated or needle-shaped, or irregularly shaped, surface coated or uncoated, porous or non-porous, charged or uncharged, and can be added to the current compositions as a

powder or as a pre-dispersion. These particulate materials may provide a wide range of functions, including but not limited to modifying skin feel, masking the appearance of certain skin characteristics such as blotchy areas, age spots, freckles, fine lines, wrinkles, and pores, absorbing excess skin sebum/oils, reducing skin shine, improving application properties of the composition, masking the color of other components of the composition, filling in skin pores, lines and wrinkles, and reducing migration of liquid materials on the skin. Preferably, particulate materials are present in the composition in levels of from about 0.01% to about 20%, more preferably from about 0.05% to about 10%, still more preferably from about 0.1% to about 5%, by weight of the composition. There are no specific limitations as to the pigment, colorant or filler powders used in the composition.

Particulate materials useful herein include but are not limited to bismuth oxychloride, sericite, mica, mica treated with barium sulfate or other materials, zeolite, kaolin, silica, boron nitride, lauroyl lysine, nylon, polyethylene, talc, styrene, polypropylene, polystyrene, ethylene/acrylic acid copolymer, sericite, aluminum oxide, silicone resin, barium sulfate, calcium carbonate, cellulose acetate, PTFE, polymethyl methacrylate, starch, modified starches such as aluminun starch octenyl succinate, silk, glass, and mixtures thereof. Preferred organic powders/fillers include, but are not limited, to polymeric particles chosen from the methylsilsesquioxane resin microspheres such as for example those sold by Toshiba silicone under the name Tospearl 145A; microspheres of polymethylmethacrylates such as those sold by Seppic under the name Micropearl M 100; the spherical particles of crosslinked polydimethylsiloxanes, especially such as those sold by Dow Corning Toray Silicone under the name Trefil E 506C or Trefil E 505C, sphericle particles of polyamide and more specifically Nylon 12, especially such as those sold by Atochem under the name Orgasol 2002D Nat C05, polystyerene microspheres such as for example those sold by Dyno Particles under the name Dynospheres, ethylene acrylate copolymer sold by Kobo under the name FloBead EA209, PTFE, polypropylene, aluminium starch ocetenylsuccinate such as those sold by National Starch under the name Dry Flo, microspheres of polyethylene such as those sold by Equistar under the name of Microthene FN510-00, silicone resin, polymethylsilsesquioxane silicone polymer, platelet shaped powder made from L-lauroyl lysine, and mixtures thereof. Especially preferred are spherical powders with an average primary particle size from 0.1 to 75 microns, preferably from 0.2 to 30 microns.

Also useful herein are interference pigments. Interference pigments, for purposes of the present specification are defined as thin platelike layered particles having two or more layers of controlled thickness with different refractive indices that yield a characteristic reflected color from the interference of typically two, but occasionally more, light reflections, form different

layers of the platelike particle. The most common examples of interference pigments are micas layered with about 50 – 300 nm films of TiO2, Fe2O3, silica, tin oxide, and/or Cr2O3. Such pigments are often peralescent. Pearl pigments reflect, refract and transmit light because of the transparency of pigment particles and the large difference in the refractive index of mica platelets and, for example, the titanium dioxide coating. Useful intereference pigments are available commercially from a wide variety of suppliers, for example, Rona (Timiron™ and Dichrona™), Presperse (Flonac™), Englehard (Duochrome™), Kobo (SK-45-R and SK-45-G) , BASF (Sicopearls) and Eckart (e.g. Prestige Silk Red). Especially preferred are interference pigments with smaller particle sizes, with an average diameter of individual particles less than about 75 microns in the longest direction, preferably with an average diameter less than about 50 microns.

Other pigments useful in the present invention provide color primarily through selective absorption of specific wavelengths of visible light, and include inorganic pigments, organic pigments and combinations thereof. Examples of useful inorganic pigments include iron oxides, ferric ammonium ferrocyanide, manganese violet, ultramarine blue, and Chrome oxide. Organic pigments can include natural colorants and synthetic monomeric and polymeric colorants. An example is phthalocyanine blue and green pigment. Also useful are lakes, primary FD&C or D&C lakes and blends thereof. Also useful are encapsulated soluble or insoluble dyes and other colorants. Inorganic white or uncolored pigments useful in the present invention, for example TiO2, ZnO, or ZrO2, are commercially available from a number of sources. One example of a suitable particulate material contains the material available from U.S. Cosmetics (TRONOX TiO2 series, SAT-T CR837, a rutile TiO2). Particularly preferred are charged dispersions of titanium dioxide, as are disclosed in U.S. Patent No. 5,997,887.

Preferred colored or uncolored non-interference-type pigments have a primary average particle size of from about 10 nm to about 100,000 nm, more preferably from about 20nm to about 5,000nm, even more preferably from about 20nm to about 1000nm. Mixtures of the same or different pigment/powder having different particle sizes are also useful herein (e.g., incorporating a TiO2 having a primary particle size of from about 100 nm to about 400 nm with a TiO2 having a primary particle size of from about 10 nm to about 50 nm).

The pigments/powders of the current invention can be surface treated to provide added stability of color and/or for ease of formulation. Non-limiting examples of suitable coating materials include silicones, lecithin, amino acids, metal soaps, polyethylene and collagen. These surface treatments may be hydrophobic or hydrophilic, with hydrophobically treatments being preferred. Particularly useful hydrophobic pigment treatments include polysiloxane treatments such as those disclosed in U.S. Patent 5,143,722.

Composition Forms

The topical compositions of the subject invention, including but not limited to lotions, milks, mousses, serums, sprays, aerosols, foams, sticks, pencils, gels, creams and ointments, may comprise a dermatologically acceptable emollient. Such compositions preferably contain from about 2% to about 50% of the emollient. As used herein, "emollient" refers to a material useful for the prevention or relief of dryness, as well as for the protection of the skin. A wide variety of suitable emollients are known and may be used herein. Sagarin, Cosmetics, Science and Technology, 2nd Edition, Vol. 1, pp. 32-43 (1972), contains numerous examples of materials suitable as an emollient. A preferred emollient is glycerin. Glycerin is preferably used in an amount of from about 0.001 to about 20%, more preferably from about 0.01 to about 15%, and even more preferably from about 0.1 to about 10% by weight of the composition.

Compositions of this invention useful for cleansing ("cleansers") are formulated with a suitable carrier (e.g., as described above, and from about 1% to about 90%, by weight of the composition, of a dermatologically acceptable surfactant).

The physical form of the cleansing compositions is not critical. The compositions can be, for example, formulated as toilet bars, liquids, shampoos, bath gels, hair conditioners, hair tonics, pastes, or mousses. Toilet bars are preferred since this is the form of cleansing agent most commonly used to wash the skin. Rinse-off cleansing compositions, such as shampoos, require a delivery system adequate to deposit sufficient levels of actives on the skin and scalp. A preferred delivery system involves the use of insoluble complexes. For a more complete disclosure of such delivery systems, see U.S. Patent 4,835,148.

The compositions of the present invention may also be in the form of cosmetics. Suitable cosmetic forms include, but are not limited to, foundations, lipsticks, rouges, mascaras, and the like. Such cosmetic products may include conventional ingredients such as oils, colorants, pigments, emollients, fragrances, waxes, stabilizers, and the like. Exemplary carriers and such other ingredients which are suitable for use herein are described, for example, in U.S. Patent No. 6,060,547.

Composition Preparation

The compositions of the present invention are generally prepared by conventional methods such as are known in the art of making topical compositions. Such methods typically involve mixing of the ingredients in one or more steps to a relatively uniform state, with or without heating, cooling, application of vacuum, and the like. The compositions are preferably prepared such as to optimize stability (physical stability, chemical stability, photostability) and/or delivery of the active materials (e.g., N-acyl amino acids, sugar amine, vitamin B_3, retinoid, phytosterol, dialkanoyl hydroxyproline, hexamidine, salicylic acid). This optimization may

include appropriate pH (e.g., less than 7), exclusion of materials that can complex with the active agent and thus negatively impact stability or delivery (e.g., exclusion of contaminating iron), use of approaches to prevent complex formation (e.g., appropriate dispersing agents or dual compartment packaging), use of appropriate photostability approaches (e.g., incorporation of sunscreen/sunblock, use of opaque packaging), etc.

Methods for Regulating Keratinous Tissue Condition

The compositions of the present invention are useful for regulating a number of mammalian keratinous tissue conditions. Such regulation of keratinous tissue conditions includes prophylactic and therapeutic regulation. More specifically, such regulating methods are directed to, but are not limited to, thickening keratinous tissue (i.e., building the epidermis and/or dermis and/or subcutaneous layers of the skin and where applicable the keratinous layers of the nail and hair shaft), preventing, retarding, and/or treating uneven skin tone by acting as a lightening or pigmentation reduction cosmetic agent, preventing, retarding, and/or treating atrophy of mammalian skin, softening and/or smoothing lips, hair and nails of a mammal, preventing, retarding, and/or treating itch of mammalian skin, preventing, retarding, and/or treating the appearance of dark under-eye circles and/or puffy eyes, preventing, retarding, and/or treating sallowness of mammalian skin, preventing, retarding, and/or treating sagging (i.e., glycation) of mammalian skin, preventing and/or retarding tanning of mammalian skin, desquamating, exfoliating, and/or increasing turnover in mammalian skin, reducing the size of pores in mammalian skin, regulating oily/shiny appearance of mammalian skin, preventing, retarding, and/or treating hyperpigmentation such as post-inflammatory hyperpigmentation, preventing, retarding, and/or treating the appearance of spider vessels and/or red blotchiness on mammalian skin, preventing, retarding, and/or treating fine lines and wrinkles of mammalian skin, preventing, retarding, and/or treating skin dryness (i.e., roughness, scaling, flaking) and preventing, retarding, and/or treating the appearance of cellulite in mammalian skin.

Applicants have surprisingly found that compositions consisting essentially of the select N-acyl amino acid compounds of the present invention are useful for the above disclosed methods as well.

Regulating keratinous tissue condition involves topically applying to the keratinous tissue a safe and effective amount of a composition of the present invention. The amount of the composition that is applied, the frequency of application and the period of use will vary widely depending upon the level of N-acyl amino acid and/or other components of a given composition and the level of regulation desired, e.g., in light of the level of keratinous tissue damage present or expected to occur.

In a preferred embodiment, the composition is chronically applied to the skin. By "chronic topical application" is meant continued topical application of the composition over an extended period during the subject's lifetime, preferably for a period of at least about one week, more preferably for a period of at least about one month, even more preferably for at least about three months, even more preferably for at least about six months, and more preferably still for at least about one year. While benefits are obtainable after various maximum periods of use (e.g., five, ten or twenty years), it is preferred that chronic applications continue throughout the subject's lifetime. Typically applications would be on the order of about once per day over such extended periods, however application rates can vary from about once per week up to about three times per day or more.

A wide range of quantities of the compositions of the present invention can be employed to provide a skin appearance and/or feel benefit. Quantities of the present compositions, which are typically applied per application are, in mg composition/cm^2 skin, from about 0.1 mg/cm^2 to about 20 mg/cm^2. A particularly useful application amount is about 0.5 mg/cm^2 to about 10 mg/cm^2.

Regulating keratinous tissue condition is preferably practiced by applying a composition in the form of a skin lotion, clear lotion, milky lotion, cream, gel, foam, ointment, paste, emulsion, spray, conditioner, tonic, cosmetic, lipstick, foundation, nail polish, after-shave, or the like which is intended to be left on the skin or other keratinous tissue for some aesthetic, prophylactic, therapeutic or other benefit (i.e., a "leave-on" composition). After applying the composition to the keratinous tissue (e.g., skin), it is preferably left on for a period of at least about 15 minutes, more preferably at least about 30 minutes, even more preferably at least about 1 hour, even more preferably for at least several hours, e.g., up to about 12 hours. Any part of the external portion of the face, hair, and/or nails can be treated, e.g., face, lips, under-eye area, eyelids, scalp, neck, torso, arms, hands, legs, fingernails, toenails, scalp hair, eyelashes, eyebrows, etc. The application of the present compositions may be done using, e.g., the palms of the hands and/or fingers, an implement, e.g., a cotton ball, swab, pad, etc.

Another approach to ensure a continuous exposure of the keratinous tissue to at least a minimum level of the N-acyl amino acid is to apply the compound by use of a patch applied, e.g., to the face. Such an approach is particularly useful for problem skin areas needing more intensive treatment (e.g., facial crows feet area, frown lines, under eye area, and the like). The patch can be occlusive, semi-occlusive or non-occlusive. The N-acyl amino acid composition can be contained within the patch or be applied to the skin prior to application of the patch. The patch can also include additional actives such as chemical initiators for exothermic reactions such as those

described in PCT application WO 9701313. The patch can also contain a source of electrical energy (e.g., a battery) to, for example, increase delivery of the N-acyl amino acid and other active agents (e.g., iontophoresis). The patch is preferably left on the keratinous tissue for a period of at least about 5 minutes, more preferably at least about 15 minutes, more preferably still at least about 30 minutes, even more preferably at least about 1 hour, even more preferably at night as a form of night therapy.

Examples

The following are non-limiting examples of the compositions of the present invention. The examples are given solely for the purpose of illustration and are not to be construed as limitations of the present invention, as many variations thereof are possible without departing from the spirit and scope of the invention, which would be recognized by one of ordinary skill in the art. In the examples, all concentrations are listed as weight percent, unless otherwise specified and may exclude minor materials such as diluents, filler, and so forth. The listed formulations, therefore, comprise the listed components and any minor materials associated with such components. As is apparent to one of ordinary skill in the art, the selection of these minors will vary depending on the physical and chemical characteristics of the particular ingredients selected to make the present invention as described herein.

Examples I – VI

A moisturizing skin cream/lotion is prepared by conventional methods from the following components.

Component	I	II	III	IV	V	VI
Phase A						
water	qs	qs	qs	qs	qs	qs
glycerol	5.0000	7.0000	7.0000	10.0000	5.0000	7.0000
phenylbenzimidazole sulfonic acid	0	0	0	0	1.2500	0
disodium EDTA	0.1000	0.1000	0.1000	0.1000	0.1000	0.1000
allantoin	0.2000	0.2000	0.2000	0.2000	0.2000	0.0000
N-undecylenoyl-L-phenylalanine	1.0000	0.5000	2.0000	0.7500	1.5000	2.0000
N-acetyl glucosamine	2.5000	2.5000	0.0000	0.0000	5.0000	0.0000
hexamidine isethionate	0.1000	0.3000	1.0000	0	0	0
triethanolamine	0.4	0.20	0.80	0.30	1.35	0.8000
sodium metabisulfite	+0.1000	0.2000	0.1000	0.1000	0.1000	0.0000
BHT	0.0150	0.0150	0.0150	0.0150	0.0150	0.0000
titanium dioxide(1)	0.2500	0.4500	0.4500	0.7500	0.5500	0.6040
niacinamide	0	2.0000	2.0000	3.5000	5.0000	5.0000
dexpanthenol	0.25	0.5000	1.0000	2.0000	1.0000	1.0000
palmitoyl-pentapeptide(2)	0	0	0.0004	0	0.0003	0.0003

Phase B						
C12-C15 alkyl benzoate	5.00	2.5000	1.5000	2.5000	0	0
caprylic/capric triglyceride	1.0	1.5000	1.5000	1.5000	1.5000	0
octyl salicylate	0	0	0	0	5.0000	0
octocrylene	0	0	0	0	1.0000	0
butyl methoxydibenzoylmethane	0	0	0	0	2.0000	0
Dipalmitoyl Hydroxyproline	0	0	1.0000	0	0	0.50
cetyl alcohol	0.5000	0.5000	0.5000	0.5000	0.5000	0.5000
tocopherol acetate	0	0.5000	0.5000	0.5000	0.5000	0.5000
sorbitan stearate/sucrose cocoate	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000
cetearyl glucoside/cetearyl alcohol	0.5000	0.5000	0.5000	0.5000	0.5000	0.5000
stearyl alcohol	0.7000	0.7000	0.7000	0.7000	0.7000	0.7000
behenyl alcohol	0.6000	0.6000	0.6000	0.6000	0.6000	0.6000
ethyl paraben	0.2000	0.2000	0.2000	0.2000	0.2000	0.2000
propyl paraben	0.1000	0.1000	0.1000	0.1000	0.1000	0.1000
PEG-100 stearate	0.1000	0.1000	0.1000	0.1000	0.1000	0.1000
sucrose polycottonseedate	0	0	0	0	0	0.6700
isohexadecane	0	0	0	0	0	3.0000
Salicyclic acid	1.5	0	0	0	0	0
PPG 15 Stearyl Ether	4	0	0	0	0	0
isopropyl isostearate	0	0	0	0	0	1.3300
polymethylsilsesquioxane	0.2500	0.5000	1.5000	0.5000	0.2500	0.2500
Phase C						
polyacrylamide/C13-14 isoparaffin/laureth-7	2.000	2.2500	2.5000	2.5000	3.0000	2.5000
Phase D						
retinyl propionate	0.0000	0.0000	0.1000	0.0000	0	0
phytosterol	1.0000	0	0.5000	0.0000	0.0000	0
green tea extract	1.0000	1.0000	1.0000	1.0000	0	0
benzyl alcohol	0.2500	0.2500	0.2500	0.2500	0.2500	0.4000
dimethicone/dimethiconol	0.5	1.0000	2.5000	0.2500	2.0000	2.0000
perfume	0.2000	0.2000	0.2000	0.2000	0.2000	0.2000

(1) titanium dioxide used is a blend of titanium dioxide in a blend of water, glycerin, ammonium polyacrylate, methyl paraben, and propyl paraben.
(2) palmitoyl-pentapeptide = palmitoyl-lysine-threonine-threonine-lysine-serine available from Sederma.

In a suitable vessel, the Phase A components are combined and mixed with a suitable mixer (e.g., Tekmar RW20DZM) and heated with stirring to a temperature of about 70 - 80°C, and this temperature is maintained. In a separate suitable vessel, the Phase B components are combined and mixed with a suitable mixer and are heated with stirring to about 70 - 75°C, and this temperature is maintained. The Phase B mixture is then added to the Phase A mixture and mixed well so as to emulsify the combination. The emulsion of Phase A and B components is

then allowed to cool to about 60° C and then the Phase C components are added to the emulsion with continuous mixing. The emulsion of Phase A, B and C components is then allowed to further cool to about 40° C, and then the Phase D components are added with mixing to the emulsion. The resulting emulsion is then milled using a suitable mill (Tekmar T-25) for about 5 minutes or until the product is uniform.

Examples VII-XI

A moisturizing skin cream/lotion is prepared by conventional methods from the following components.

Component	VII	VIII	IX	X	XI
Phase A					
water	qs	qs	qs	qs	qs
allantoin	0.2000	0.2000	0.2000	0.2000	0.2000
disodium EDTA	0.1000	0.1000	0.1000	0.1000	0.1000
ethyl paraben	0.2000	0.2000	0.2000	0.2000	0.2000
propyl paraben	0.1000	0.1000	0.1000	0.1000	0.1000
BHT	0.0150	0.0150	0.015	0.0150	0.0150
dexpanthenol	1.0000	0.5000	1.0000	1.0000	1.0000
glycerin	7.5000	10.000	15.000	7.5000	5.0000
N-undecylenoyl-L-phenylalanine	2.0000	0.5	1.0000	4.0000	1.0000
hexamidine isethionate	0.0000	0.1000	0.1000	0.0000	1.0000
niacinamide	0	3.5000	5.0000	2.0000	2.0000
palmitoyl-pentapeptide(1)	0	0	0	0.0004	0.0003
Phenylbenzimidazole sulfonic acid	0	0	0	0	1.0000
benzyl alcohol	0.2500	0.2500	0.2500	0.2500	0.2500
triethanolamine	0.8	0.2	0.40	1.60	1.0
green tea extract	1.0000	1.0000	1.0000	1.0000	1.0000
N-acetyl glucosamine	0.0000	5.0000	2.0000	1.0000	5.0000
sodium metabisulfite	0.1000	0.1000	0.1000	0.1000	0.1000
Phase B					
cyclopentasiloxane	15.000	15.000	18.000	15.000	15.000
titanium dioxide	0.5000	0.5000	0.7500	0.5000	0.5000
Phase C					
C12- C15 alkyl benzoate	1.5000	0	0	1.5000	1.5000
Dipalmitoyl Hydroxyproline	0	1.0000	0	0	1.0000
Salicyclic Acid	1.5	0	0	0	0
PPG-15 Stearyl Ether	4	0	0	0	0
vitamin E acetate	0.5000	0	1.0000	0.5000	0.5000
retinyl propionate	0.000	0	0	0.2000	0.2000
phytosterol	0.0000	.0000	1.0000	5.0000	3.0000
Phase D					
KSG-21 silicone elastomer (2)	4.0000	4.0000	5.0000	4.0000	4.0000
Dow Corning 9040 silicone elastomer	15.000	15.000	12.000	15.000	15.000
Abil EM-97 Dimethicone Copolyol (3)	0.5000	0	0	0.5000	0.5000
polymethylsilsesquioxane	2.5000	2.5000	2.0000	2.5000	2.5000

fragrance	0.2000	0.2000	0.2000	0.2000	0.2000

(1) palmitoyl-pentapeptide = palmitoyl-lysine-threonine-threonine-lysine-serine available from Sederma.
(2) KSG-21, an emulsifying silicone elastomer available from Shin Etsu
(3) Abil EM-97 available from Goldschmidt Chemical Corporation

In a suitable vessel, the Phase A components are blended together with a suitable mixer (e.g., Tekmar model RW20DZM) and mixing is continued until all of the components are dissolved. Then, the Phase B components are blended together in a suitable vessel and are milled using a suitable mill (e.g., Tekmar RW-20) for about 5 minutes. The Phase C components are then added to the Phase B mixture with mixing. Then, the Phase D components are added to the mixture of Phases B and C and the resulting combination of Phase B, C, and D components is then mixed using a suitable mixer (e.g., Tekmar RW-20) for about 1 hour. Then, Phase A is slowly added to the mixture of Phases B, C, and D with mixing. The resulting mixture is then continually mixed until the product is uniform. The resulting product is then milled for about 5 minutes using an appropriate mill (e.g., Tekmar T-25).

Examples XII - XVII:

Moisturizing silicone-in-water creams/lotions are prepared by conventional methods from the following components:

	XII	XIII	XIV	XV	XVI	XVII
Water Phase:						
Water	qs	qs	qs	qs	Qs	qs
Glycerin	3	5	7	10	15	10
Disodium EDTA	0.1	0.1	0.05	0.1	0.1	0.1
Niacinamide	0	0.5	3.5	3	5	3
N-Undecylenoyl-L-phenylalanine	1	0.5	2	0.75	1.0	2
Triethanolamine	0.4	0.2	0.8	0.3	0.6	0.8
D-panthenol	0.5	0.1	1.0	0.5	1.5	0.5
GLW75CAP-MP (75% aq. TiO2 dispersion)[1]	----	0.4	----	----	----	----
Hexamidine isethionate	0	0.1	----	1.0	0.1	----
Palmitoyl-pentapeptide[2]	----	----	----	----	0.0003	----
N-acetyl glucosamine	0	----	2	----	5	----
Silicone/Oil Phase:						
Cyclomethicone D5	10	5	5	10	7.5	10
Dow Corning 9040 silicone elastomer[3]	----	10	5	5	7.5	5
KSG-15AP silicone Elastomer[4]	5	----	5	5	7.5	5
Dimethione/dimethiconol	----	2	2	1	2	1
Dimethicone 50 csk	1	----	----	----	----	----
Zinc Oxide	0	0	0	0	0	3
Retinyl Propionate	0	0.2	0	0	0.1	0
Salicyclic Acid	1.5	0	0	0	0	0
PPG 15 Stearyl Ether	4					

Phytosterol	----	----	----	0.1	----	0.1
Vitamin E Acetate	----	0.5	0.1	0.1	----	0.1
Thickener:						
Polyacrylamide/C13-14 isoparaffin/laureth-7	2.5	2.5		----	----	3
Sodium acrylate/sodium acryloyldimethyl taurate copolymer/isohexadecane/ polysorbate 80	----	----	----	3	----	----
Acrylates/C10-30 alkyl acrylates crosspolymer	----	----	0.6	----	0.5	----
Dipalmitoyl Hydroxy-Proline Premix:						
Water	0	0	8.85	0	4.40	0
Triethanolamine	0	0	0.15	0	0.075	0
Dipalmitoylhyroxyproline	0	0	1	0	0.50	0
Additional Ingredients:						
Triethanolamine	----	----	----	----	0.6	----
PTFE	----	0.5	----	----	----	----
Polymethylsilsequioxane	----	0.5	1.0	----	----	----
Polyethylene	----	0.5	----	----	1.0	----
Flamenco Summit Green G30D[5]	----	----	1.0	----	----	----
Prestige Silk Red[6]	----	----	----	1.0	1.0	1.0
Total:	100%	100%	100%	100%	100%	100%

[1] GLW75CAP-MP, 75% aqueous titanium dioxide dispersion from Kobo
[2] Palmitoyl-lysine-threonine-threonine-lysine-serine available from Sederma
[3] A silicone elastomer dispersion from Dow Corning Corp
[4] A silicone elastomer dispersion from Shin Etsu
[5] Titanium dioxide and tin oxide coated mica green interference pigment from Engelhard
[6] Titanium dioxide coated mica red interference pigment from Eckart

In a suitable vessel, combine and mix the water phase ingredients until uniform. In a separate suitable container, combine and mix the silicone/oil phase ingredients until uniform. Separately, if present, prepare the dipalmitoyl hydroxyproline premix by combining the premix ingredients in a suitable container, heating to about 70°C while stirring, and cooling to room temperature while stirring. Add half the thickener and then the silicone/oil phase to the water phase and mill the resulting emulsion (e.g., with a Tekmar T-25). Add the remainder of the thickener, the dipalmitoyl hydroxyproline premix if present, and then the remaining ingredients to the emulsion while stirring. Once the composition is uniform, pour the product into suitable containers.

While particular embodiments of the present invention have been illustrated and described, it would be obvious to those skilled in the art that various other changes and modifications can be made without departing from the spirit and scope of the invention. It is therefore intended to cover in the appended claims all such changes and modifications that are within the scope of this invention.

All documents cited in the Background, Summary of the Invention, and Detailed Description of the Invention are, in relevant part, incorporated herein by reference; the citation of any document is not to be construed as an admission that it is prior art with respect to the present invention.

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